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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/574,626	05/19/2000	Jose Remacle	VANM159.001AUS	7665

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EXAMINER	
ZHOU, SHUBO	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/574,626	REMACLE ET AL.	
	Examiner	Art Unit	
	Shubo "Joe" Zhou	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10/6/03*. 11/28/03
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

Response to RCE

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/14/03 and 11/28/03, i.e. the IDS documents have been received and considered.

It is noted that the request for an RCE is not accompanied by any amendments and/or arguments in response to the previous Office action mailed on 5/30/03.

Applicants are reminded that, as noted in the Advisory action mailed 12/6/02 and in the Office action mailed 5/30/03, the after-final amendments filed 11/8/02 have not been entered. The CPA filing procedure includes express abandonment of the prior application along with continuing prosecution thereafter, but the prior non-entered amendments are entered "only" if requested. Therefore, the claims that are under current consideration are the claims with amendment filed 3/5/02.

Claims 1, and 3-33 are pending and under consideration.

Claim Rejections-35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102(e) that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 6, 28 and 33 are rejected under 35 U.S.C. § 102(e) as being anticipated by Lockhart et al. (US patent No: 6,344,316, Issued Feb. 5, 2002, Filed June 25, 1997).

The claims are drawn to a method of using a high density nucleic acid array for identifying and quantifying a target nucleic acid in a biological sample.

Lockhart et al. disclose a method for detecting nucleic acids using oligonucleotide array. The method comprises putting into contact target nucleic acids with capture molecules, i.e. oligonucleotides, which are fixed upon a surface of solid support according to an array with a density of more than about 60 different oligonucleotides per cm2. See columns 2 and 5. The method also comprises labeling the targets with different means including colorimetric labels such as colloidal gold. The binding of the oligonucleotides with targets leads to formation of precipitate. See column 24. It would have been readily recognized by an ordinary skill in the art that the amount of colorimetric precipitates on gold particles indicates the amount of binding and that colloidal gold involved colorimetric labeling forms precipitate at the location of the binding. Lockhart et al. disclose that the sample for the target is in a biological sample. See column 2, line 34. It should be pointed out that while Lockhart et al. does not literally recite the term "precipitate", it would have been well known in the art that the method of colormetric detection involving colloidal gold actually involves precipitation of the gold particle at the location of binding between the nucleic acids.

This rejection is reiterated from the previous Office action mailed 6/5/02 and that mailed 5/30/03 and maintained for reasons of record.

Claim Rejections-35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1, 7-9, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lockart et al. (US patent No6,344,316, Issued Feb. 5, 2002, Filed June 25, 1997) in view of Van Ness et al. (US patent No. 6,027,890, Issued Feb. 22, 2000, Filed July 22, 1997).

The claims are drawn to a method of using a high density array for identifying and quantifying a target compound in a biological sample, wherein the binding between the capture molecule on the array and the target compounds is a reaction between an antigen and an antibody or a receptor and its ligand.

Lockhart et al. disclose a method for detecting nucleic acids using oligonucleotide array. The method comprises putting into contact target nucleic acids with capture molecules, i.e. oligonucleotides, which are fixed upon a surface of solid support according to an array with a density of more than about 60 different oligonucleotides per cm2. See columns 2 and 5. The method also comprises labeling the targets with different means including colorimetric labels such as colloidal gold. The binding of the oligonucleotides with targets leads to formation of precipitate. See column 24. Lockhart et al. disclose that the sample for the target is in a biological sample. See column 2, line 34. However, Lockhart et al. do not show in their method that the binding between the capture molecule on the array and the target compounds in the

sample is a reaction between an antigen and an antibody or a receptor and its ligand, as required in the instant claims.

Van Ness et al. disclose a method for detecting biomolecules using array involving the formation of precipitates and determining the presence of precipitates with means such as a CCD-linked microscope (column 76, lines 31-44). The binding between the target and capture molecule can be hybridization between two nucleotide sequences (column 74 and column 76, lines 9-29), binding between proteins/antigens and antibodies, as required by the instant claim 7, or receptor-ligand pair, as required by the instant claim 9 (see column 2). In regard to claim 9, which requires that the presence of the precipitate is detected by reflection, adsorption of light, Van Ness et al. detect the presence with a microscope equipped with a CCD camera. It would have been readily recognized by one of ordinary skill in the art that the image is obtained by reflection of a light beam upon the precipitate, as is recognized in the art that light reflection is one of the working principles in such a microscope equipped with a CCD camera. In regard to claim 28, which requires that the precipitate is formed on the surface of the particle associated with the target compound, the method of Van Ness et al. makes use of the well-known system of biotin-streptavidin/horseradish peroxide (column 76) and the precipitate is formed using a precipitating substrate linked to the biotin-streptavidin system. Thus, it would have been well known in the art that such a precipitate would be formed on the surface of a particle associated with the target compound, as required in the instant claims.

Since Lockhart et al. provide high density array and state that the method is rapid and simple to apply, and since Van Ness et al. provide methods for detecting not just nucleic acids, but also others like proteins/antigens, antibodies, or receptor-ligands using an array, one of ordinary skill in the art would have been motivated to combine the references to generate a method of using high density array and used for different biomolecules including nucleic acids, antigen/antibody and receptor-ligands. Since both references provide detailed procedures and

guidance, there would have been a reasonable expectation of success. Thus, the claimed invention would have been obvious to one of ordinary skill in the art at the time the invention was made.

This rejection is reiterated from the previous Office action mailed 6/5/02, and maintained for reasons of record.

Claims 1, 3-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abouzied et al. (Journal of AOAC International, Vol. 77, No. 2 (MAR-APR), pp. 495-501, 1994) in view of Howard III et al. (IDS document: EP 0646784A1, 05-04-95) and Van Ness et al. (US patent No. 6,027,890, Issued Feb. 22, 2000, Filed July 22, 1997), and in further view of Roth et al. (US patent # 5,902,727, Issued May 11, 1999, application filing date: Sep. 4, 1996) and Terstappen et al. (US patent # 5,646,001, July 8, 1997).

Abouzied et al. disclose a method of simultaneously screening and detection of multianalyte using membrane strips, which is interpreted as the array of the instant claims. The method comprises the steps of contacting analytes (interpreted as the target compounds in the instant claims), with multiple antibodies (interpreted as the capture molecules of the instant claims) to let them bind; precipitation being formed on the membrane upon binding; detection and quantification of the precipitates by light reflection and video image analysis. The binding as disclosed is a reaction between an antigenic structure and its corresponding antibody as is required in the instant claims and the antibody and its corresponding antigen can be interpreted at a broad sense, as a receptor and its corresponding ligand, as required of the instant claims. The presence of the precipitates is detected by both visual detection of the color intensity by

reflection, as required in the instant claims, and for quantification, image is taken by a CCD video camera and is converted into digital form (abstract and Experimental, pages 495-497). Abouzied also disclosed an apparatus, termed "a computer-assisted multianalyte assay system", for the detection and/or quantification of multianalytes, which apparatus comprises detection and/or quantification device including camera, and a computer to collect results including the images taken by the camera, as required in the instant claims (Figure 1 and page 497). A video-digitizing board is equipped with the CCD camera and is interpreted as the sensor as required in the instant claims. A computer program for performing the above steps is stored on a computer readable medium, which is in the broad sense the printed paper copy of the publication.

Abouzied et al. does not explicitly disclose the use of a strip of at least 20 discrete regions per cm^2 for analyzing the multianalytes.

Brown et al. disclose an invention including a substrate with a surface having a microarray of at least 10 distinct polynucleotide or polypeptide biopolymers in a surface area of about 1 square cm (see column 4, lines 16-23). It would have been obvious that one of ordinary skill in the art would have been motivated to choose any density that falls the disclosed at least 10, such as at least 20 discrete regions per square cm.

Howard III et al. disclose apparatus and methods of using video test strip reader to analyze analytes. The apparatus disclosed comprises CCD camera equipped with illumination sources and computer system (see page 5) . The apparatus also comprises an image handler coupled to the video imager and a video reader. The video handler includes a signal converter that converts or digitizes the analog signal from the video imager into a digital signal representing the image (see the paragraph bridging pages 5 and 6 and paragraph 2 of page 6). The imager handler, video imager, and the video reader are interpreted as the "sensor(s) provided with camera(s)" as required in the instant claims. The signal converter (page 11, line 3) is also interpreted as such sensor. Howard III et al.'s apparatus can also evaluate information such as

bar code as required in the instant claims (see page 7, lines 55-56). The apparatus disclosed uses its processor to initially calibrate and produce reflectance reference matrices by reading the reflectance value for the viewing field, i.e. the first reference standard as required in the instant invention, and measure the reflectance for that test area in addition to the test pad, i.e. the second reference standard in the instant invention. Howard III et al. do not disclose but motivate the use of more than one illuminant sources specially arranged , spaced and controlled, as required in the instant claims, in order to "evenly illuminate the viewing field...in order for video imager...to accurately measure the color or reflectance of the various test pads" and "the illumination source is preferably a DC light source with a control feedback to minimize light fluctuations" (see page 5, lines 51-55)and the motivation is witnessed further by the phrase "any illumination variations on the viewing area" (page 11, line 20). Howard III et al. also suggest the use of other light sources including infra-red light, as required in the instant claims (see page 7, lines 5-10).

Abouzied et al. and Howard III et al. do not disclose using multiple cameras in the system as required in the instant claims. However, it would be obvious to ordinary people in the art to use more than one camera to simply expedite the performing process. They also do not disclose the detection of the presence of the precipitate by using metallic compound, magnetic metallic compound, the reduction of silver in the presence of colloidal gold particles, etc., as required in the instant claims. However, these are common means used in different assays in the prior arts as summarized in Roth et al.: "the binding of such probes to the target substance is typically detected microscopically by the use of direct labeled probes such as fluorophores, enzyme conjugates, gold particles and the like" and "recent advances in detection systems have improved the sensitivity and resolution of the probe localization and include such methods as immunogold with silver intensification, peroxidase-anti-perxidase..." (see column 1). Terstappen et al. also summarize the use of metallic and magnetic metallic compounds in biochemical separation and detection (see the bridging paragraph between columns 2 and 3). Thus, it would be obvious for

one to combine these techniques with the teachings of Abouzied et al. and Howard III et al. to practice the detection of precipitates to take advantage of the increased sensitivity and resolution.

Claims 27, and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Abouzied et al. (Journal of AOAC International, Vol. 77, No. 2 (MAR-APR), pp. 495-501, 1994) in view of Van Ness et al. (US patent No. 6,027,890, Issued Feb. 22, 2000, Filed July 22, 1997), and Gingeras et al. (US patent # 6,228,575, issued May 8, 2001, filed Feb.7, 1997).

Abouzied et al. disclose a method of simultaneously screening and detection of multianalyte using membrane strips (interpreted as the array of the instant claims) as summarized in the abstract, comprising the steps of contacting analytes (interpreted as the target compounds in the instant claims), with multiple antibodies (interpreted as the capture molecules of the instant claims) to let them bind; precipitation being formed on the membrane upon binding; detection and quantification of the precipitates by light reflection and video image analysis. The binding as disclosed is a reaction between an antigenic structure and its corresponding antibody as is required in the instant claims and the antibody and its corresponding antigen can be interpreted at a broad sense, as a receptor and its corresponding ligand, as required of the instant claims. The presence of the precipitates is detected by both visual detection of the color intensity by reflection, as required in the instant claims, and for quantification, image is taken by a CCD video camera and is converted into digital form (abstract and Experimental, pages 495-497). Abouzied also disclosed an apparatus, termed "a computer-assisted multianalyte assay system",

for the detection and/or quantification of multianalytes, which apparatus comprises detection and/or quantification device including camera, and a computer to collect results including the images taken by the camera, as required in the instant claims (Figure 1 and page 497). A video-digitizing board is equipped with the CCD camera and is interpreted as the sensor as required in the instant claims. The camera is a device for reading information on the array. A computer program for performing the above steps is stored on a computer readable medium.

Van Ness et al. disclose a method of detecting biomolecules using array and an apparatus for the detection comprising the array on a solid support, a microscope and a CCD camera (column 76). It would have been obvious to one of ordinary skill in the art that such a CCD camera would have been linked to a computer with a program to recognize such images of discrete regions on the array in order to process the images taken by the camera, and to detect/quantitate the target compounds.

Bar code would have been widely used in the art of bioassays. For example, Gingeras et al. disclose a chip-based species identification using array and bar code and an apparatus comprising a computer system and bar code reader (see Figures 14, 15, and 32 and column 7). One of ordinary skill in the art would have been motivated to combine the references and use a bar code reader to take advantage of its convenience and speed.

In summary, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to combine the teachings and/or motivations of Abouzied et al., Van Ness et al., and Gingeras et al. to make and use the claimed invention.

Conclusion

No claim is allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on 571-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst William Phillips whose telephone number is 571-272-0548, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shubo (Joe) Zhou, Ph.D.
Patent Examiner

ARDIN H. MARSCHEL
PRIMARY EXAMINER